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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,486	12/05/2003	David J. Ecker	IBIS0060-100 (DIBIS-0012U)	9735
58057	7590	07/27/2006	EXAMINER	
MEDLEN & CARROLL LLP 101 HOWARD STREET SUITE 350 SAN FRANCISCO, CA 94105			FREDMAN, JEFFREY NORMAN	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/728,486

Applicant(s)

ECKER ET AL.

Examiner

Jeffrey Fredman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 12 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 27-29,31-38 and 50-87 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 27-29,31-38 and 50-87 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12/27/03
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Claim Interpretation***

1. As a preliminary issue, the claims must be interpreted before proceeding with the prior art analysis. While the phrase "base composition signature" is defined at page 26 of the specification, the phrase "base composition" appears repeatedly in the claims and specification but no definition of this term was found. Therefore, the term is broadly read to encompass any mode of determination of molecular mass, including mass determinations by sizing on gel electrophoresis, as well as mass spectrometry, which is the clearly preferred mode of analysis.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 27, 28, 32-34, 36-38, 50, 69, 70, 72-76, 79, 80, 81, 84 and 85 are rejected under 35 U.S.C. 102(b) as being anticipated by Hurst et al (Rapid Comm. Mass Spectrom. (1996) 10:377-382).

Hurst teaches a method of claims 27, 69 and 75 of identifying a pathogenic bioagent in sample (see page 377, column 1), comprising:

*(a) amplifying a plurality of segments of nucleic acid of said pathogen with a plurality of primer pairs to obtain a plurality of amplification products (see page 378,*

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table I, and page 378, column 2, where PCR was performed using two sets of primer pairs, one directed to the 5S rRNA gene and one directed to the mip gene fragment)

*(b) determining the base compositions of at least two members of said plurality of amplification products wherein said base compositions identify said pathogen in said sample* (see page 379, figure 1, where Hurst performs MALDI-TOF on both PCR products to determine base composition as the mass of the PCR product, and shows that this is a feasible method of detecting Legionella).

With regard to claims 28, 70, 81, Hurst teaches detection of a bacterial pathogen (see page 379, figure 1, where Legionella is detected).

With regard to claims 32-34, 76, Hurst teaches the use of specific primers that are genus and species specific (see page 378, table 1).

With regard to claim 36, Hurst teaches the base compositions of both the mip and 5S rRNA pcr products (see page 379, figure 1).

With regard to claims 37, 72, 73, 79, 80, Hurst teaches the use of MALDI-TOF (see abstract).

With regard to claims 38, 74, 84, Hurst teaches analysis of the 5S rRNA gene using primers directed to that gene (see page 378, table 1).

With regard to claims 50, 85, Hurst teaches analysis of the mip gene, which encodes a protein involved in virulence (see page 378, table 1).

4. Claims 27-29, 31-35, 38, 50-60, 63-71, 74-78 and 81-87 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoffman et al (Arch. Virol. (2001) 146:2275-2289).

Hoffman teaches a method of claims 27, 53, 69 and 75 of identifying a pathogenic bioagent in sample (see page 2278, where influenza is the bioagent), comprising:

*(a) amplifying a plurality of segments of nucleic acid of said pathogen with a plurality of primer pairs to obtain a plurality of amplification products (see page 2278, subheading "Design of oligonucleotides for RT-PCR" and pages 2278-2281, which detail a PCR reaction that was performed using eight sets of primer pairs, directed to the eight segments of the influenza virus)*

*(b) determining the base compositions of at least two members of said plurality of amplification products wherein said base compositions identify said pathogen in said sample (see page 2281, figure 3, where the base composition in terms of mass is determined by gel electrophoresis).*

With regard to claims 28, 54, 70, 81, Hoffman teaches detection of a viral pathogen (see page 2281, figure 3, where Influenza virus is detected).

With regard to claims 29, 55, 71, 82, Hoffman teaches the use of tissue sample (see page 2277, where tissue from embryonated eggs is used and see page 2276, where virus isolation occurs from the throat of mammals).

With regard to claim 31, 56, 57, 83, Hoffman teaches that samples can be obtained from mammals and teaches the virus infects humans (see page 2276).

With regard to claims 32-34, 58-59, 76, Hoffman teaches the use of specific primers that are viral genus specific (see page 2278).

With regard to claim 35, 60, 77, 78, Hoffman teaches detection of viral subtypes using the primers (see figure 4, page 2282 and figure 5, page 2283 (and table 3) where primers specific for each subtype were used).

With regard to claims 38, 63, 74, 84, Hoffman teaches analysis of all of the genes of Influenza A, including any housekeeping genes (see page 2281, figure 2, where all of the eight segments of Influenza A are amplified).

With regard to claims 50, 51, 64, 65, 85, 86, Hoffman teaches analysis of all of the influenza A virus genes, including genes involved in virulence and the Influenza polymerase genes, PB1, PB2 and PA which form a heterotrimer (see page 2281, figure 2).

With regard to claim 66, 68, Hoffman teaches the use of eight primer pairs (see page 2281, figure 2).

With regard to claim 52, 67, 87, Hoffman teaches analysis "In pandemic situations where a new virus subtype emerges, we could either use the plasmid collection already available or quickly generate plasmids iwth the same or similar sequences, and use it to develop antiviral therapies (i.e., vaccines). Thus, a universal primer set is a powerful tool that can be used in classic and reverse genetics methods to prevent and contain future influenza A epidemics and pandemics (see page 2287)."

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 36, 37, 61, 62, 72, 73, 79 and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman et al (Arch. Virol. (2001) 146:2275-2289) in view of Koster (WO 98/20166).

Hoffman teaches a method of claims 27, 53, 69 and 75 of identifying a pathogenic bioagent in sample (see page 2278, where influenza is the bioagent), comprising:

*(a) amplifying a plurality of segments of nucleic acid of said pathogen with a plurality of primer pairs to obtain a plurality of amplification products* (see page 2278, subheading "Design of oligonucleotides for RT-PCR" and pages 2278-2281, which

detail a PCR reaction that was performed using eight sets of primer pairs, directed to the eight segments of the influenza virus)

*(b) determining the base compositions of at least two members of said plurality of amplification products wherein said base compositions identify said pathogen in said sample* (see page 2281, figure 3, where the base composition in terms of mass is determined by gel electrophoresis).

With regard to claims 28, 54, 70, 81, Hoffman teaches detection of a viral pathogen (see page 2281, figure 3, where Influenza virus is detected).

With regard to claims 29, 55, 71, 82, Hoffman teaches the use of tissue sample (see page 2277, where tissue from embryonated eggs is used and see page 2276, where virus isolation occurs from the throat of mammals).

With regard to claim 31, 56, 57, 83, Hoffman teaches that samples can be obtained from mammals and teaches the virus infects humans (see page 2276).

With regard to claims 32-34, 58-59, 76, Hoffman teaches the use of specific primers that are viral genus specific (see page 2278).

With regard to claim 35, 60, 77, 78, Hoffman teaches detection of viral subtypes using the primers (see figure 4, page 2282 and figure 5, page 2283 (and table 3) where primers specific for each subtype were used).

With regard to claims 38, 63, 74, 84, Hoffman teaches analysis of all of the genes of Influenza A, including any housekeeping genes (see page 2281, figure 2, where all of the eight segments of Influenza A are amplified).



With regard to claims 50, 51, 64, 65, 85, 86, Hoffman teaches analysis of all of the influenza A virus genes, including genes involved in virulence and the Influenza polymerase genes, PB1, PB2 and PA which form a heterotrimer (see page 2281, figure 2).

With regard to claim 66, 68, Hoffman teaches the use of eight primer pairs (see page 2281, figure 2).

With regard to claim 52, 67, 87, Hoffman teaches analysis "In pandemic situations where a new virus subtype emerges, we could either use the plasmid collection already available or quickly generate plasmids with the same or similar sequences, and use it to develop antiviral therapies (i.e., vaccines). Thus, a universal primer set is a powerful tool that can be used in classic and reverse genetics methods to prevent and contain future influenza A epidemics and pandemics (see page 2287)."

Hoffman teaches PCR to analyze and compare the viral subtypes but does not teach mass spectrometry or base composition signatures.

Koster teaches a method for detecting a single nucleotide polymorphism in an individual using molecular mass measurements such as MALDI TOF (page 14, for example), by determining the molecular mass of said amplification product using mass spectroscopy (page 13, line 1 and page 157, lines 10-29 and example 19) and comparing the molecular mass to the molecular mass of said region in an individual known to have said polymorphism, where if said molecular masses are the same then

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said individual has said polymorphism (page 13, lines 2-5 and page 158, lines 1-29, where Koster expressly compares patient 1 to a negative control and example 19).

With regard to claims 36, 37, 61, 62, 72, 73, 79 and 80, Koster expressly teaches comparison of base compositions with both modified and unmodified products (see page 66, for example, as well as page 105, table II and pages 69-70). At page 105, table II, Koster provides the base composition of three different PCR products determined by MALDI-TOF. Further, Koster specifically discusses using base composition to analyze mutations as discussed on page 70, where Koster notes "MS can also be used to determined full or partial sequences of larger DNAs; this can be used to detect, locate, and identify new mutations in a given gene region."

In particular, Koster expressly teaches the use of MALDI-TOF for diagnosis of bacterial or viral infections (see pages 73-79). Koster exemplifies this analysis in Example 5.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry method of Koster in the analytical method of Hoffman since Koster states "In another embodiment, an accurate sequence determination of a relatively large target nucleic acid, can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments to determine the sequence of the larger target nucleic acid (see page 75, line 26 to page

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76, line 2).” So an ordinary practitioner would have been motivated to detect the PCR products of Muddiman with the base composition Mass spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

### ***Double Patenting***

7. Claims 27-29, 31-38 and 50-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 59,60,62,63,66,69-76 and 79-94 of copending Application No. 10/156,608. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined. Therefore, the species of claims 59,60,62,63,66,69-76 and 79-94 of copending Application No. 10/156,608 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 27-29, 31-38 and 50-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-19 and 29-38 of copending Application No. 10/660,997. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is

determined. Therefore, the species of claims 14-19 and 29-38 of copending Application No. 10/660,997 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 27-29, 31-38 and 50-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 14, 17, 28-44 of copending Application No. 10/660,996. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined. Therefore, the species of claims 1-10, 14, 17, 28-44 of copending Application No. 10/660,996 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 27-29, 31-38 and 50-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-27, 30-34, 44-55 of copending Application No. 10/660,122. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is

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determined. Therefore, the species of claims 23-27, 30-34, 44-55 of copending Application No. 10/660,122 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

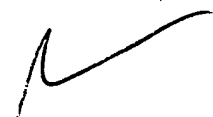
12. Given the large number of related cases which show up on PALM, many of which are abandoned, Applicant is requested to comply with 37 CFR 1.56 by identification of copending applications, particularly applications close to issuance, which raise double patenting issues.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jeffrey Fredman  
Primary Examiner  
Art Unit 1637

